DKMS Stiftung Leben Spenden

Project Summary

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Toxin-free antibody-based conditioning for hematopoietic stem cell transplantation

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Sickle cell disease (SCD) is a devastating inherited blood disease affecting 8 million people worldwide. Stem cell transplantation can enable cure of SCD patients essentially by “rebooting” their blood-forming system using stem cells from a healthy donor. However, the treatment with chemotherapy and irradiation, or “conditioning,” that patients must undergo before transplantation causes short- and long-term toxicities that impact quality of life, lifespan, and fertility. Therefore, an urgent and unmet need exists to make stem cell transplantation safer so that this lifesaving therapy can be more widely used to treat SCD and other inherited blood diseases.

My project seeks to address this unmet need by developing and evaluating conditioning strategies for stem cell transplantation using antibodies rather than chemotherapy or irradiation, which we hypothesize will enable transplantation of healthy donor stem cells with fewer toxicities. However, existing antibody-based conditioning strategies have undesirable side effects on red blood cells (RBC), making them particularly unsuitable for use in RBC diseases like SCD. In this project, we will develop novel antibody-based conditioning regimens that avoid RBC toxicities and evaluate their ability to target mouse and human stem cells and make space for transplantation. We will then apply these conditioning regimens to enable transplant and cure in a humanized mouse model of SCD. We envision that these studies will provide important proof-of-principle data and experimental tools for future studies which will advance our ultimate goal of bringing antibody-based conditioning to the clinic.